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ROUND TRIP FROM SPACE

Melvin Calvin

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ABSTRACT

Whence came life on the surface of the earth? Whether or not a complete answer to this question may be found within the context, and content, of modern science, may be a moot question. It is our purpose to see how far we can devise an answer, and how satisfactory it may be, within that context.

We trace a path from the primitive molecules of the primeval earth's atmosphere condensed from space, through the random formation of more or less complex organic molecules, using the available energy sources of ultraviolet light, ionizing radiation or atmospheric electrical discharge, through the selective formation of complex organic molecules via autocatalysis, finally, to the information-transmitting molecule which is capable of self-reproduction and variation. In addition, somewhere, either during the course of this Chemical Evolution, or perhaps succeeding it, a system has been evolved in which the concentration of the reaction materials was retained in a relatively small volume of space, leading to the formation of cellular structures. Man is about to send back into space some bits of the dust from whence it originally came. It is thus not only timely but more significant than ever before to ask again the question: What are the probabilities that cellular life as we know it may exist at other sites in the universe than the surface of the earth?

We can assert with some degree of scientific confidence that cellular life as we know it on the surface of the earth does exist in some millions of other sites in the universe. We thus remove life from the limited place it occupied, as a rather special and unique event on one of the minor planets, to a state of matter widely distributed throughout the universe.

Man's adventure into space, which is about to begin, is a necessary aspect of evolution and of human evolution in particular. It is an activity within the capability of this complex organism, man, and it must be explored as every other potentially-useful evolutionary possibility has been. The whole evolutionary process depends upon each organism developing to the greatest extent, every potential. It is the particular function of the university to facilitate this development of the uniquely human potential of understanding and control -- to lead the species in its new exploration as well as serving it in transmitting its established patterns.

ROUND TRIP FROM SPACE*

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On such an occasion as this, the beginning of a new phase in the life of a university, we stop for a moment to review progress that men have made in their various fields of thought and action. One can choose a variety of ways of accomplishing this review. One could, for example, gather together and enumerate the specific accomplishments, both intellectual and material, in the areas of biology and chemistry. I have chosen, rather, to illuminate these accomplishments by seeking to answer a question which men have asked since first they thought, but to answer it particularly in the light of our progress in biology and chemistry in the last century.

The question of which I speak may be formulated in many ways. One way is to ask the question: Whence came life on the surface of the earth? Another would be, in more personal terms as Pearl Buck has asked it: "Who are we, by whom were we made, and how, and for what purpose?" Whether or not a complete answer to these questions may be found within the context, and content, of modern science remains a moot question.

It is my purpose this evening to see how far we can devise an answer, and how satisfactory it may be, within that context. It becomes clear immediately that we will be dealing not only with the advances of biology that have occurred, but all of the contiguous sciences -- physics, chemistry, geology, astronomy and the like. However, our primary point of view will be that of biology and chemistry.

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In trying to provide this answer we will, of necessity, have to review the accomplishments, particularly of these areas, both in their practical, concrete knowledge, as well as the impact they have, and will have, on man's view of himself and his place in the universe. At every point of our discussion, we will limit ourselves to asking questions, and providing answers, which, at some point, may be susceptible of observational, or experimental, test.

WHAT IS LIFE?

Since we have phrased the question in terms of "the origin of life", we presumably have a clear conception of what we mean by the term "life." There is very little doubt but what, on the ordinary level of human experience, there is no difficulty in distinguishing that which lives from that which does not. However, when we explore this notion to try to determine precisely what it is, or to be even more specific, what qualities we must devise, in order to produce something which lives from something which does not with no help from a living agency save the hand of man, the question becomes somewhat more ambiguous. For example, there are many qualities which we have no difficulty in attributing to a living organism. It is able to reproduce itself, to respond to an environmental change (i.e., "come in out of the rain,"), to transform energy into order (sunshine into a leaf, leaf into a hair), to change and remember the change, etc. While many of these individual characteristics may be duplicated in systems in space, one or more at a time, it is only when a sufficiently large collection of them appears in a single system in space that we call that system alive.

Thus, the definition of life takes on the arbitrariness of the definition of any particular point on a varying continuum, and precisely where that point will fall on the line of time and evolution will depend a good deal upon who is watching the unfolding of that line.

With this last remark, we have introduced the basic notion of evolution which, since its precise formulation exactly one hundred years ago by Darwin and Wallace, has pervaded all of science. In fact, most of what I have to say this evening could be formulated in terms of a long extra/polation backward in time of the notions that were so ably expressed by Darwin and Wallace in 1858, but which they do not extend very far back, either in geologic time or certainly in cosmic time[1].

As most of you know, for a period of over sixty years any serious discussion of the question of the origin of life was not indulged in by scientists, particularly by experimental scientists. In fact, it was considered a disreputable kind of activity. It is interesting to examine what some of the reasons for this might have been. One certainly (and perhaps a dominant reason) was the dictum of a contemporary of Darwin's (1809-1882), a chemist, Louis Pasteur (1822-1895), who, in 1864, quite clearly provided an answer to the question which, for many decades previous, had been the subject of much discussion, namely, the possibility of the spontaneous generation of life on earth today. Pasteur quite clearly, and definitely, established, in his experiments of 1864, that it was impossible on the earth today, under controlled conditions, to demonstrate the appearance of living material except through the agency, or as offspring of, other living material. While Pasteur opposed the Darwinian formulation of evolution, largely on religious grounds, I suspect that he either knew consciously, or felt instinctively, that the Darwinian doctrine was conceptually in conflict with his experimental conclusion.[2] A search of the works of Darwin has revealed no mention of his opinion of the conclusions that Pasteur reached in 1864.

In any case, for over sixty years thereafter, as I mentioned earlier, there appeared practically no serious discussion of the origin of life, or spontaneous generation. Between the publication in 1870 by Alexander Winchell,

a professor of geology, zoology and botany at the University of Michigan, of a book entitled, "Sketches of Creation"[3] and the statement by J.B.S. Haldane, professor of biology, in 1928,[4] there appears to be no serious attempt to answer the question of the origin of life within the context of the science of the period.

The hiatus came to an end with the recognition, by Professor Haldane, that the dictum of Pasteur was not in conflict with the backward extrapolation of the doctrine of evolution as expounded by Darwin and Wallace, if one recognizes that at the time that spontaneous generation must have occurred, according to the evolutionary extrapolation of Darwin and Wallace, there was not, by definition, any living thing on the surface of the earth. Therefore, it was possible, in the prebiotic time, to accumulate large amounts of organic material generated by nonbiological processes. This, of course, cannot take place on the surface of the earth today, since there exist everywhere on the earth's surface organisms, both micro and macro, which would transform any such organic material immediately it is formed, even in small amounts. Thus, the apparent conflict of concept between the backward extrapolation of evolution and the dictum of "no life save from life" can be, and has been, resolved.[5] Since that time, that is, 1928, it has become increasingly popular, amongst scientists (experimental and otherwise) to examine the question of the origin of life from the scientific point of view. In fact, it has become so popular that within the last 18 months there have been held at least two conferences in the United States and one international conference on the subject.

THE TIME SCALE

It seems wise to have a look at the time we have in which to accomplish this total evolution of life. Here, in the first of our figures (FIGURE 1) we can see something of the order of magnitude of the time with which we have to deal related to the geologic history of the earth. The earth was formed

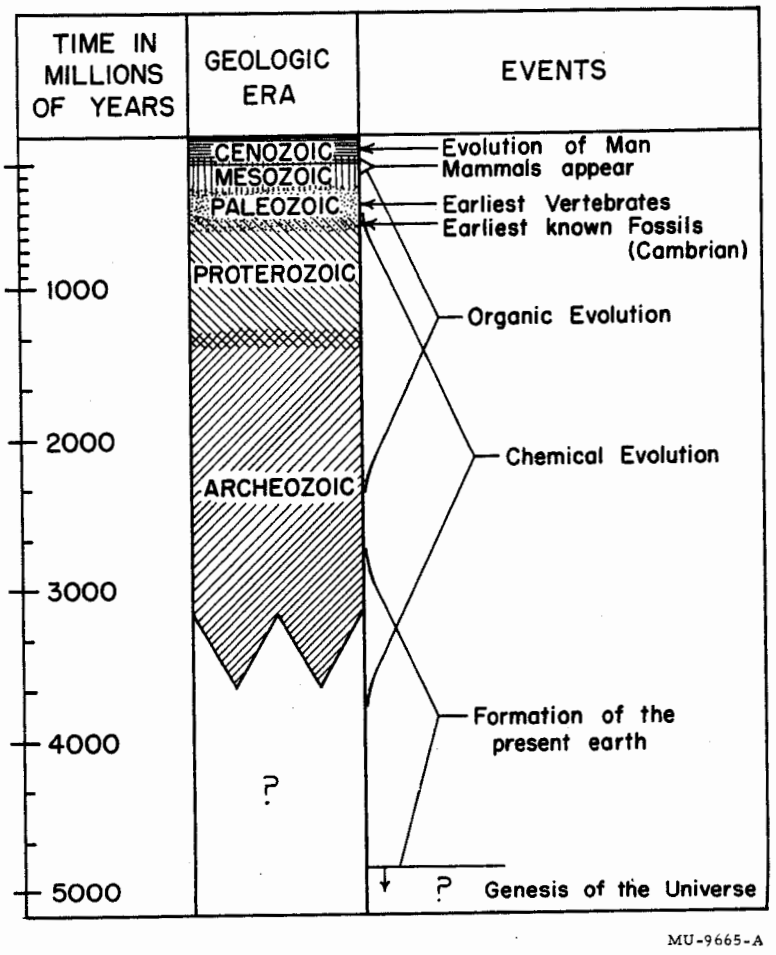


FIGURE 1

The Time Scale for Total Evolution

from matter in space some four to seven billion years ago. Whether this was an aggregation of cosmic dust or a primeval explosion remains a matter of some controversy and will come up again a bit later in our discussion. However, that terrestrial history itself is only some five billion years in extent seems to be well established. You can see in FIGURE 1 that we have marked the evolutionary periods on the surface of the earth to correspond with the known geologic eras.

The earliest period might be spoken of as the period of evolution of the present earth. Overlapping this, and including the Archezoic and Proterozoic geologic eras (some four to two billion years ago) is the principal period of which we will speak, namely, the period of Chemical Evolution. It was during this time that the formation of more complex organic molecules from simple ones occurred by nonbiological methods which we will try to describe in a moment. Overlapping the period of Chemical Evolution we have marked the period of Organic Evolution , up to the present day. This period of Organic Evolution is the one whose later part is recorded in the form of fossils. However, for its greatest part, beginning some time in the Archezoic period and extending through the Proterozoic period, there is no fossil record. This period of Organic Evolution of the soft-bodied living organisms, which left no fossils, constitutes by far the longer fraction of the period which we call Organic, or Biological, Evolution. Finally, at the very apex of the entire structure exists a point which we call the Evolution of Man. This constitutes only something like the last million years of geologic time, and it is clear that this represents a minute fraction of the time period with which we have to deal.

THE PRIMITIVE ATMOSPHERE

It should be noted that one of the prerequisites of all of the speculation about the origin of life is that there exists a means of gradually producing relatively complex organic substances by nonbiological processes. This question

is susceptible to experimental investigation, and has been investigated by a variety of experimental scientists, with positive results. It is clear that in order to test any chemical process as a possible means of generating organic material by nonbiological means, we must first know what the raw materials for these chemical processes must be. This, of course, entails some knowledge of the nature of the atmosphere of the primeval earth. This, in turn, requires a concept of the mode of formation of the earth and the solar system in which it exists. There have been a wide variety of hypotheses on this point. For example, Shapley in his recent discussion, lists some fifteen different hypotheses with regard to the origin of the earth and the solar system.[6a,b] In any case, one thing is common to all of the hypotheses, namely, that the earth did have a solid crust and some kind of a gaseous atmosphere. The question that is open to some discussion is whether that crust and atmosphere was primarily oxidizing or primarily reducing in character. In the former case, the dominant partners for all the atoms are oxygen atoms, while in the latter they are hydrogen atoms.

It is clear that no matter what concept one accepts for the origin of the earth, the atmosphere itself must have been made up of relatively simple molecules such as nitrogen, ammonia, possibly carbon dioxide, methane, hydrogen and the like. A group of these molecules is shown in the first row of FIGURE 2. There has been considerable discussion as to whether the oxidized molecules or the reduced molecules constituted the major portion of this atmosphere. It would appear that the present consensus favors the reduced group. In any case, experiments have been done with both types of atmosphere.

RANDOM ORGANIC SYNTHESIS -- THE BEGINNING OF CHEMICAL EVOLUTION

The agents which have been called upon to produce the initial transformations have nearly all been of the high-energy type -- ultraviolet radiation, electrical discharge, radiation from radioactivity of earth-bound minerals, or radiation coming to us from outer space in the form of cosmic rays.[5] Since it

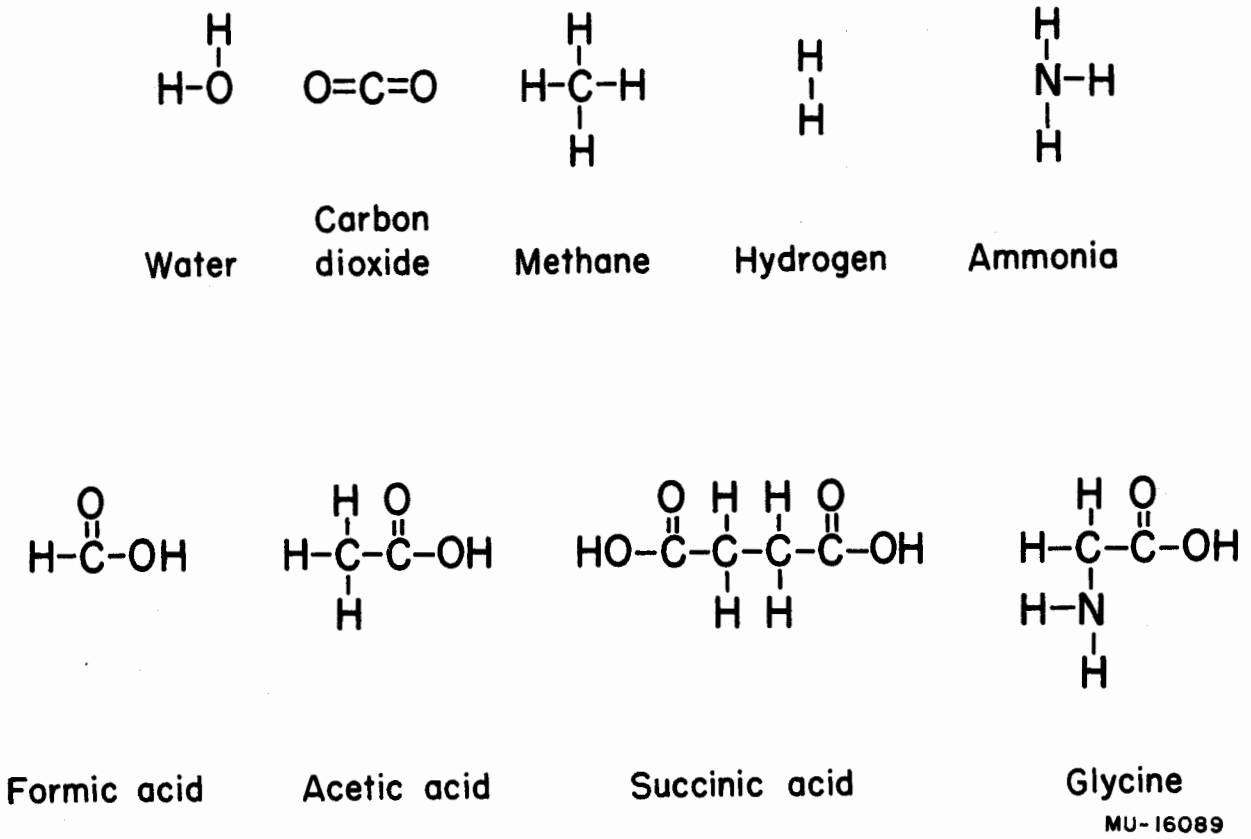


FIGURE 2

Primeval and Primitive Organic Molecules

appears that all of the concepts of the earth's formation involve the absence of molecular oxygen from its primeval atmosphere, the intensity of ultraviolet light which impinged on the surface of the earth in its early days was considerably greater than it is today. So, some of the earliest experiments designed to determine whether more complex organic molecules, containing carbon-carbon bonds, could be formed were done using the ultraviolet light as the source of the energy. They were described by Haldane as early as 1928 and they have been since checked in a variety of laboratories throughout the world. The primitive carbon compounds used in most of these experiments were already partly reduced, such as carbon monoxide, formic acid, or formaldehyde.[4]

In 1951, in our laboratory, experiments were again instituted to determine the usefulness of high-energy radiations, such as those which might be derived from the natural radioactive materials present in relatively high concentrations in the primitive earth, or from cosmic radiations coming in from space.[7] Here, the primitive carbon compounds were of the more oxidized type, strictly speaking, carbon dioxide. However, molecular hydrogen was also present in these experiments. The partial reduction of carbon from the completely oxidized form of carbon dioxide to a partly reduced form, such as formic acid or formaldehyde, was observed. In addition, new carbon-carbon bonds were apparently formed upon irradiation of aqueous solutions of such carbon compounds, leading to compounds such as oxalic acid and acetic acid, shown in the second row of FIGURE 2.

Still more recently, beginning with the premise that the primeval atmosphere was of a reducing character, experiments were undertaken which were designed to test the effectiveness of electrical discharge in the upper atmosphere (a reduced atmosphere) to create materials more closely resembling those which are presently used in biological activities.[8] Here the compounds used

as starting materials were water vapor, methane, ammonia and hydrogen. As you see, these were primarily the reduced forms of each of the elements, that is, the elements of oxygen, nitrogen, carbon, attached only to hydrogen. When an electric discharge was passed through such a mixture, one indeed did get a large variety of more complex materials, particularly those known as amino acids, of which the simplest, glycine, is shown in the figure. It is perhaps worthwhile to point out that having first reduced the one-carbon compound in the high-energy experiment and then formed a two-carbon compound by connecting two carbon atoms in the form of acetic acid, it was possible to demonstrate the generation of succinic acid, a four-carbon compound, resulting from the combinations of two molecules of acetic acid, by irradiation with high-energy radiations such as those which one might obtain from radioactive materials. It is interesting to note that these latter experiments, as well as the first ones of 1951, were done using a cyclotron rather than natural sources of radioactivity because of the high intensities of ionizing radiation which could be obtained.

One suggestion of a very different type was among the early ones used, since the elementary chemistry was already well known. This chemistry begins with metallic carbides,[5] which, on contact with water, will produce a variety of hydrocarbons such as methane and acetylene (the latter the familiar process used in the older miner's lamps). Some of these gases are of such a character that if they come into contact at high enough concentration with any of a variety of mineral surfaces, they will combine with each other to produce large, complex molecules, sometimes with very specific configurations.[9] The metal carbides used to start such a process generally require high temperatures for their formation, and it will therefore be necessary to suppose either that the earth began very hot or that it has had at least some places in, or on, it that were hot enough to form such carbides and later deliver them to the cooler surfaces. There appears to be no geologic evidence for the primary existence of such carbides in the deep rocks.

Very nearly all of these processes which we have just described for the generation of new carbon-carbon and carbon-nitrogen bonds and the creation of more complex molecules from simpler ones are processes which depend upon the primary disruption of the simple molecule into an active fragment; followed by the random combination of those active fragments into something more complex. As the material present in the atmosphere and on the crust of the earth is gradually changed from the simple to the complex, these methods of transformation will not select between the simple and complex and are just as prone to destroy by bond breakage the products of their initial activity as they are to create new ones. It is from here that we must now call upon some method of selective construction of molecules.

THE EVOLUTION OF CATALYSTS -- ENZYMES

To do this we need only to call upon the phenomenon of autocatalysis, well known to chemists.[10a] This phenomenon occurs whenever the product of any chemical transformation has the property (catalytic) of influencing the rate of its own formation. It is somewhat surprising that this phenomenon was not long ago utilized in such discussions as these, since it is, in essence, the very fact and form of the mechanism of all selective evolutionary processes, namely, the selective superiority of any form to reproduce itself that will give rise to a transformation of material into that particular form.

Thus, it is easily apparent from FIGURE 3 that of three possible transformations which A might undergo, namely, to B, to C or to D, it will undergo more frequently the transformation to D because D itself is a better catalyst for that transformation than it is for the others. Therefore, eventually the random processes which gave rise to A will not be quite so completely random in their further effectiveness. They will, in this case, tend to produce D rather than B or C from A. In general, the selective process of autocatalysis, and in higher evolution as well, is not an "all or none" process as we have just desribed

it, but rather one of a matter of degree. Thus, the actual situation is more likely to be that all three substances, B, C and D, are all catalysts for their own formation, but the most efficient is the one which will eventually supersede the others.

It is of interest to examine how this sort of chemical selectivity might have functioned in the development of an extremely important biological material which is widely distributed today. This class of material is represented by that which gives the red color to blood cells and the green color to leaves. It constitutes a very important class of organic substances known by the name of porphyrins. We have already seen how the simple precursors to porphyrins, succinic acid and glycine, might be formed (and, indeed, were formed) by a random process from the primeval carbon-containing molecules. Now we have available to us a method of tracing the route by which these two precursors eventually become porphyrins in present-day living material, and some of the essential steps in that series are shown in FIGURE 4.[11]

Underneath the center sequence are indicated, by arrows, a number of possible points where the catalytic function of iron might paly a role. For example, iron may play a part in the combination of succinic acid and glycine to start with, or in the decarboxylation of the primarily-formed keto adipic acid which is the second compound in the center row, or, finally, in one of the several steps which are necessary to convert the delta-aminolevulinic acid into the macrocyclic, or large ring, compound known as protoporphyrin No. 9 at the right-hand end of the figure. We already know that a number of these steps are definitely catalyzed by iron, but what is more important is that some of them are much more readily induced to go by the iron ion after it has been encased in the porphyrin No. 9, as shown by the dotted circle in the porphyrin than they are by the bare iron ion. Such an iron porphyrin is a much better catalyst for

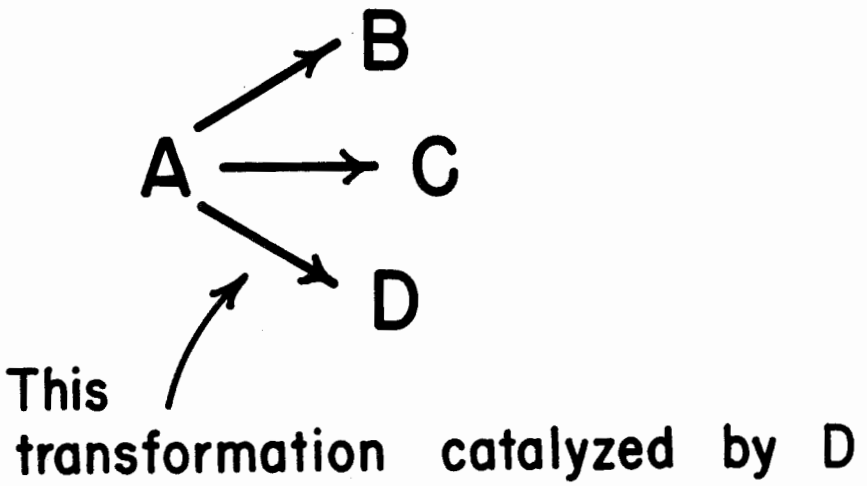


FIGURE 3

Autocatalysis as the Means of Chemical Selection

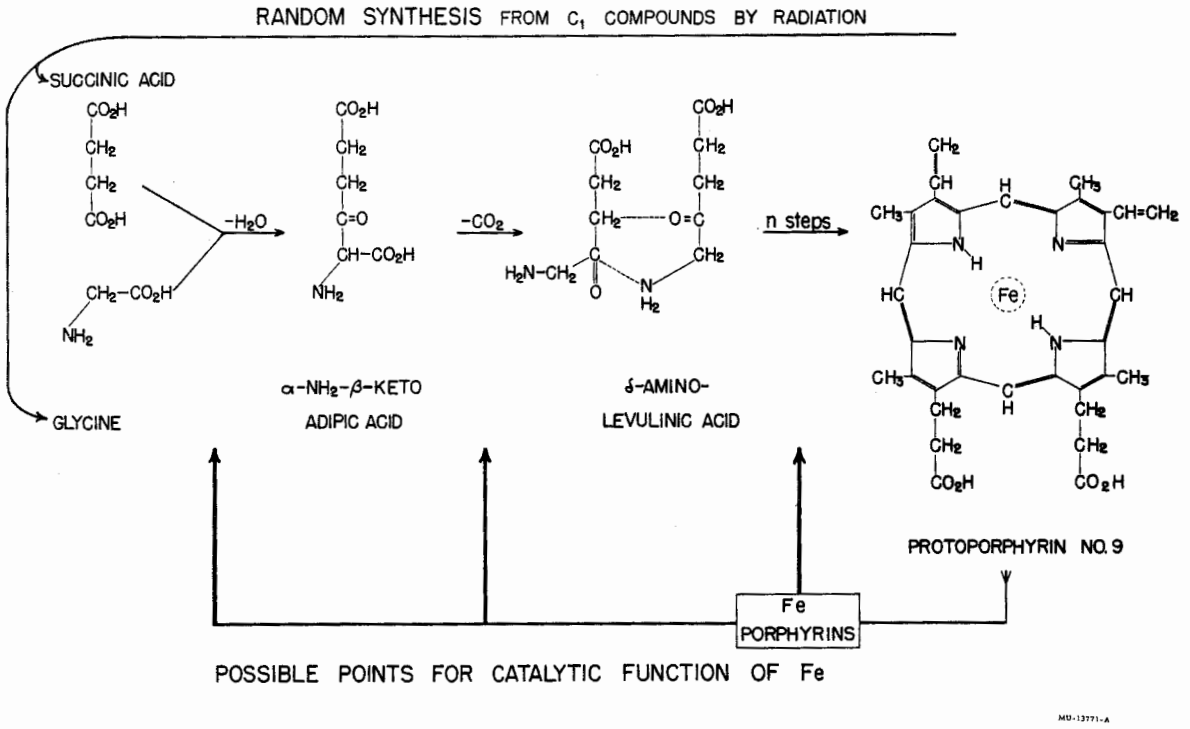


FIGURE 4

Biosynthesis of Porphyrin and the Evolution of the Catalytic Functions of Iron

several of the steps leading to its own formation than is the bare iron ion itself. Furthermore, it is almost certainly a better catalyst for the conversion of the levulinic acid toward the porphyrin than for the competitive conversion of the glycine back toward the carbon dioxide whence it came. Thus it is clear that the route from succinic acid and glycine to the porphyrin, once the porphyrin has been formed, will be greatly facilitated by the incorporation of iron into it, thus bringing a good deal more of the succinic acid and glycine into this particular, and important, form.

The process of the development of the catalytic function of iron does not and has not stopped at this point. When the iron compound is built into a protein (a macromolecule made by the combination of many amino acids), its catalytic efficiency may be increased still more. Beyond this, the variety of chemical changes in which it may assist can be increased and the efficiency of its function diversified.

Other atoms and groups of atoms having rudimentary catalytic powers can be developed into the highly efficient and specific catalysts which we know as enzymes in even the simplest of modern organisms, by exactly analogous processes of chemical selction by autocatalysis. And it is almost certainly no "accident" that these enzymes are all proteins. For it is only the proteins as a class that offer the combination of simplicity of formation(peptide bond) with practically an infinite variety of chemical function(R groups).[12] (FIGURE 5).

FROM CHAOS TO ORDER -- MOLECULAR CRYSTALLIZATION

So far, all of the processes of which we have spoken have been described as taking place in a rather dilute solution, with the molecules randomly arranged. The development of a complex material under such circumstances could not go very far. Two further stages of change seem to be required: (1) the ordering of the molecules in some rather specific array and (2) the concentration of the formed substances into relatively small packages. Which of these two processes took place first, or whether they were indeed successive or simultaneous

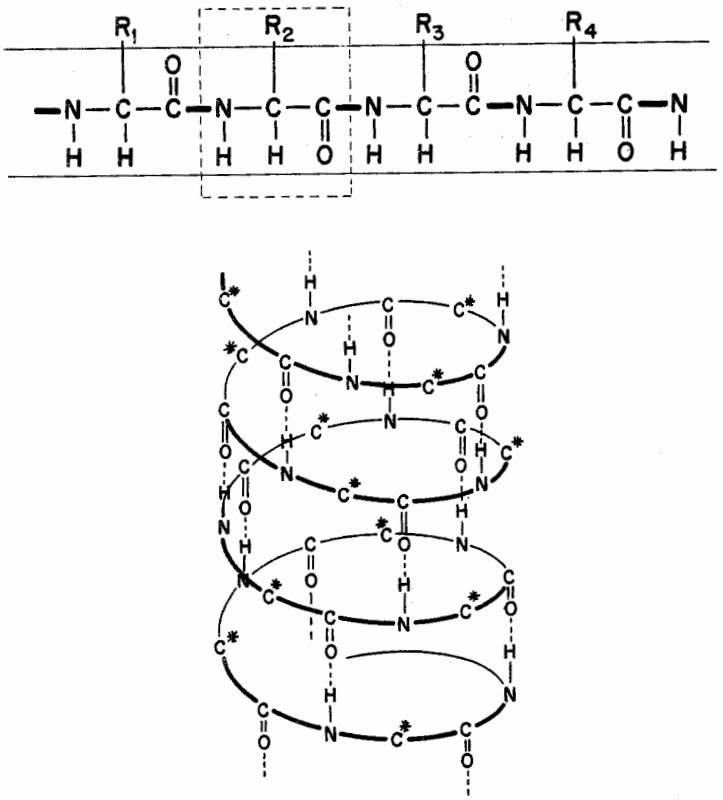
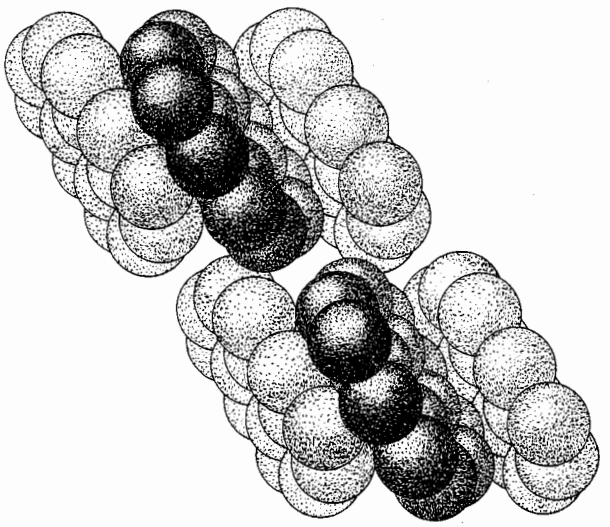


FIGURE 5
Protein Structure: Simple Structural Principles and Variety of Chemical Reactivity

developments, is hard to say. However, that both of them took place we do know, and that there exist mechanisms for each of these processes to take place we can alos demonstrate in the laboratory.

One type of molecule, for example, with which we are constantly dealing, both in the laboratory and as a result of present-day biological action, is the large, flat so-called aromatic molecule. The porphyrin that we have just mentioned constitutes one such, and there are many others. Such molecules, when they reach a certain minimal level of concentration in aqueous solution, will tend to drop out of that aqueous solution. However, they will not drop out in a random way. Because of their peculiar flat shape, they will tend to drop out in an arrangement in which the molecules are piled one on top of the other, much like a pack of cards. If one throws a pack of cards in the air and allows them to fall out of the air, onto the floor, it is unlikely that they will fall standing on edge. They will, of course, practically all (if not all) land flat, one on top of the other, becuase of their peculiar shape. This kind of phenomenon illustrates the way in which large, flat molecules tend to come out of solution in crystals. FIGURE 6 shows a diagrammatic drawing of a simple crystal of a rather simple flat molecule, and here you can see the result of the tendency of such molecules to pile up, one on top of the other.[10b]

I use this particular type of example with a purpose in mind. The reason is that much of the information that present-day living organisms carry with them and can transmit to their offspring in the form of genetic material, is made up, or seems to be contained, in an ordered array of such flat molecules as this. The additional feature that one must add to this piling-up of flat molecules is that they are not independent, as the group of cards was, but that they are all tied together along an edge, as though the group of cards were tied together by a double string. The example of the flat units that we will use here will be the pairs of complemnetary bases as they are found in



A packing drawing of the anthracene structure projected on its b face.

FIGURE 6

Packing of Flat Molecules in a Crystal

desoxynucleic acid (DNA), the material of which the chromosomes are constructed. FIGURE 7 shows these pairs as they occur: thymine paired with adenine and cytosine paired with guanine by virtue of their peculiar structure which places certain of their hydrogen atoms between oxygen and/or nitrogen atoms on the complementary molecule. These four molecules, and one other very closely related to thymine, are themselves formed from the same primitive precursors described in FIGURE 2(succinic acid, glycine, formic acid, carbon dioxide and ammonia). Along either edge of these flat units you can see the sugar-phosphorus chain which corresponds to the string-card analogy which I spoke of a moment ago.

Because of their peculiar aromatic type of structure these base pairs will tend to line up one above the other. This tendency will, of course, be increased because they are not independent of each other but tied together by the sugar-phosphate ribbons. In actual fact, the structure of desoxynucleic acid (DNA) seems to be such a flat piling up of the nucleoside bases with the sugar-phosphate ribbons twisted in a spiral around the outside as shown in the next figure (FIGURE 8).

CONCENTRATION AND LOCALIZATION -- THE FORMATION OF A CELL

The other aspect of which we spoke a moment ago, which must obtain, is the concentration into relatively small volumes in space of these organic materials, leading ultimately to the formation of cells as we now know them as the units of living matter. It is at this point thatour information and our analogies are most diffuse. However, a number of physical-chemical processes have been called on to participate in the development of the living cell. First among these is the appearance of surface layers, or boundary layers, such as one sees in a soap bubble. Here we are quite familiar with mechanisms for producing a relatively stable and well defined boundary layer between two phases. Another phenomenon which is much less familiar to us, is known by the name of coacervation and has been called upon as a primary

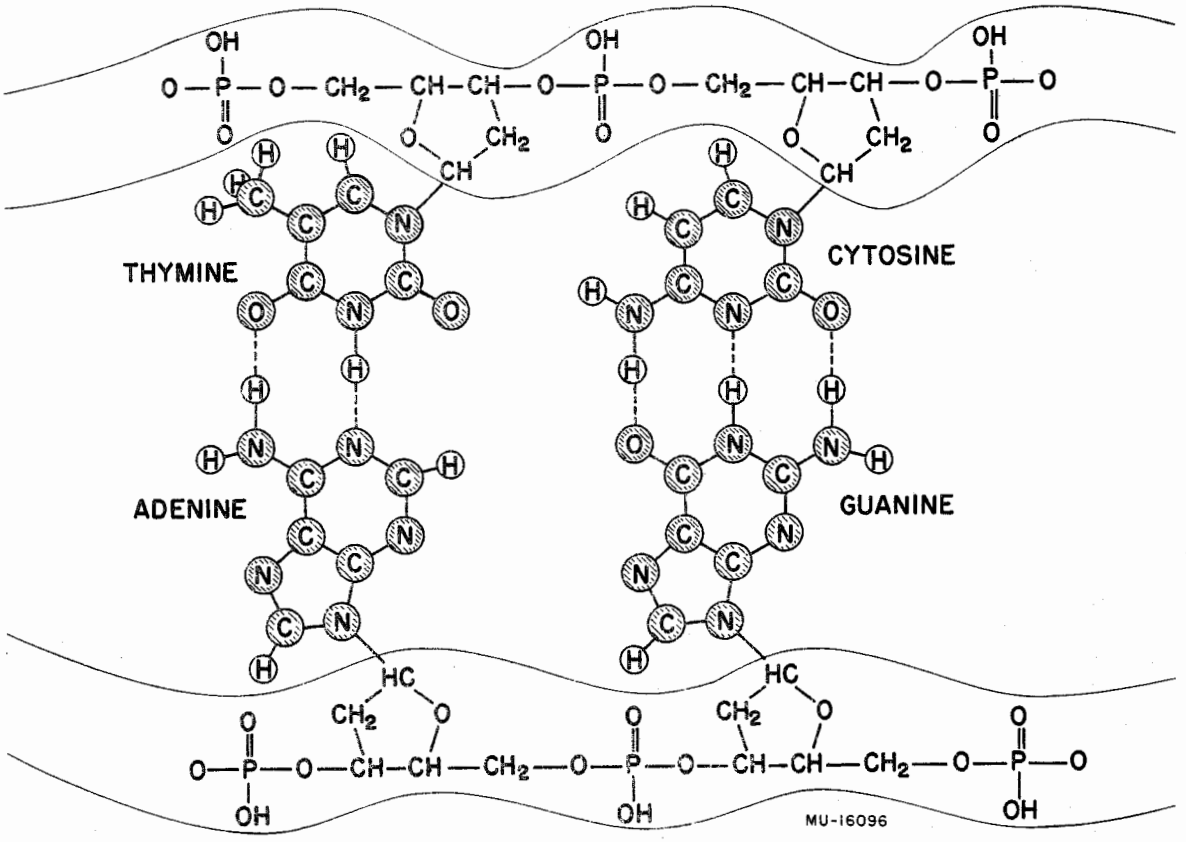


FIGURE 7

Molecular Drawing of the Components of Desoxynucleic Acid -- Genic Material

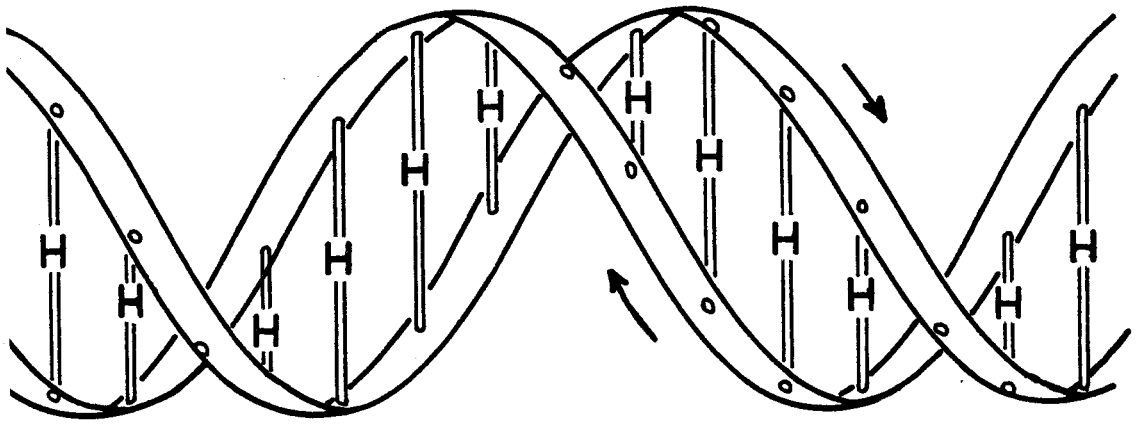


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FIGURE 8

Double Helix Model for Desoxynucleic Acid (DNA)[13]

phenomenon leading to the development of local concentration and cellular structures.[5] This phenomenon is dependent upon the ability of giant molecules in water solution to separate out from the dilute water solution into relatively more concentrated phases, or droplets, suspended in the more dilute water solution around them. Beyond this, the giant molecules tend to pack themselves in ordered arrays, provided they, themselves, have ordered structures.

While the knowledge of the interaction of giant, or macro, molecules, both synthetic and natural, has made great strides in the last decade or two, we are still only at the beginning of our investigation of systems of macromolecules of sufficient complexity to provide us with the kind of information we would like to have for the present purposes. However, it seems to me that already enough information is available to us to be able to say with confidence that the basic kinds of physical-chemical processes upon which we will have to draw in order to describe the evolution of the cellular structure are already at hand.

THE SELECTION OF THE PILOT -- DNA

That characteristic which is most frequently invoked as the prime attribute of living material is the ability to reproduce and mutate. Very frequently in discussions of the origin of life, attempts are made to define that certain point in time before which no life existed and after which we may speak of "living" things, as that point at which an organic unit, be it a molecule or something bigger, came into existence which could generate itself from existing precursors and which could sustain and propagate a structural change. Since we can be confident that genetic information is transmitted today in the environment of a cell by the chemical substance known as desoxynucleic acid (DNA), of which we have already spoken, it seems reasonable to seek in this structure the clues to the mutable self-reproducing molecule, or unit.[13]

It should be pointed out that while we are in the habit of thinking of the nucleoprotein molecules which constitute the chromosomes and viruses (DNA and RNA, ribonucleic acid) as containing all the information required to produce its entire organism, this is not strictly true. These structures may be said to contain information only in relation to, and exhibitable through, a proper environment. Thus it is possible to keep a bottle containing only virus particles (say DNA) indefinitely, just as any other organic chemical, and the question of whether it is alive or not would not arise. The moment these particles find themselves in a suitable organic medium (such as may be found in any of a variety of cell cytoplasms), this information makes itself apparent and the virus multiplies. There are thus other constituents in the modern cell which contain indispensable information but under direction of the nucleoprotein of the chromosomes.

While a chemical model[14] operating in one dimension has been described which is able to control the behavior of a mixture of precursor units as it goes on to form a larger material, it is only in recent months that the ability to separate the controlling information-carrying units from the energy-transforming units and to demonstrate that information can indeed be carried by the desoxynucleic acid particles has been achieved.[15]

You will recall that the DNA, or chromosomal material, is made up of a linear array of only four units, represented in FIGURE 7, by the four bases (adenine, thymine, cytosine and guanine) and that the controlling information about the organism (at least a modern post-Cambrian cell) is contained in some kind of linear array of these units. In the past few years it has been possible to isolate from various living organisms, particularly bacteria, a catalyst (enzyme), which, when placed into a solution containing all four of these units in an active form, that is, as their triphosphates, was able to induce their com-

bination into some particular linear array of bases to produce a particular variety of desoxynucleic acid. Which particular DNA was formed depended entirely upon the presence of a very small amount of so-called "starter" which had to be added to this mixture. If this starter were obtained from one type of cell, that particular type of desoxynucleic acid would be formed; from some other type of cell, another type of DNA would appear.[16]

Still more recently, it has been possible to make a synthetic desoxynucleic acid, consisting of only two of these bases, in particular the thymine and adenine.[17] This synthetic DNA presumably has no counterpart in nature today and yet when this synthetic material is given as a"starter" to the reaction mixture, as previously described, that particular two-base desoxynucleic acid, made up of only thymine and adenine, is produced. The catalyst which is able to do this seems to be the protein-like material constructed of amino acids in the way proteins usually are. Although little is yet known about the nature of this catalyst (enzyme) it will almost certainly be related to the simpler compounds and elements whose more primitive catalytic abilities constitute the basis for its action. This is exactly analogous to the relationship between the catalytic ability of simple iron ions and that of the highly effective iron proteins, as described in FIGURE 4.

We have thus traced a path from the primitive molecules of the primeval earth's atmosphere condensed from space, through the random formation of more or less complex organic molecules, using the available energy sources of ultraviolet light, ionizing radiation or atmospheric electrical discharge, through the selective formation of complex organic molecules via autocatalysis, finally, to the information-transmitting molecule which is capable of self-reproduction and variation. During the course of this process we have, naturally, made use of the organic materials which have been produced in high-energy form via these various energy-yielding routes. In addition, somewhere, either during the course

of this Chemical Evolution or perhaps succeeding it, a system was evolved in which the concentration of the reaction materials was retained in a relatively small volume of space, leading to the formation of cellular structures.

PLOTTING THE COURSE -- BIOSYNTHETIC PATHWAYS

During this entire course we have made use of the randomly-formed molecules, followed by a chemical kind of selection. The ultimate production of the information-carrying molecules depended upon the preferred presence of their constituent units, for example, nucleoside triphosphates or "active" amino acids. It is clear that as the efficiency of transformation is increased by chemical or early biotic evolution, all of these precursors will have been used up, and a mechanism will have to be devised for the regeneration of those precursors by more specific chemical routes than those originally used. We can see these very specific biosynthetic routes in the living organism of today.

The last ten to twenty years, since the application of tracer techniques particularly, has exposed to us the wide variety of relatively complex biosynthetic sequences, an illustration of which we had in FIGURE 4 leading to the porphyrin, and which appear to be a sequence of reactions directed toward a particular end. The usefulness of any intermediate step does not become apparent until the final product is formed. Such sequences, on an organismic level, have led to a variety of teleological theories about the nature of evolution. However, on the molecular level it is possible to see the way in which complex, apparently directed, biosynthetic sequences arose by the operation of the ordinary laws of physics and chemistry, including the idea of autocatalysis as the basis of selection.

This was pointed out by Horowitz some years ago when he recognized that once having formed a useful material into an "organism", which could transmit its information to its offspring, this process would continue so long as precursors were available for this "organism" to use for its reproduction.[18]

However, eventually it was clear that one or another or these precursors would become exhausted. That particular organism which could adapt itself by a random variation to make the missing precursor from molecules which still remained available to it would, of course, survive, provided the knowledge of how it was done could be transmitted; all the others would die out. Thus, we would now have lengthened the chain of synthesis by one step, but in a backward direction toward the simpler precursors. By extrapolating this back, eventually to carbon dioxide, one can get the very complex and what appear to be totally directed syntheses from the very simplest of all carbon compounds.

THE ULTIMATE FUEL -- PHOTOSYNTHESIS

We have remaining one additional attribute which is always associated with living material and which is very frequently called upon as a prerequisite to life, namely, the ability to use energy-yielding chemical reactions to create order out of disorder. Ultimately, of course, the large-scale evolution of living organisms to the extent that we are now familiar with it, could not take place until the invention of photosynthesis, that is, the coupling of the ability of certain molecules to absorb solar energy, to the ability of certain other molecules to use this energy for the synthesis of the necessary structures. Here it is almost certain that the ability to synthesize had long been evolved before the ability to couple the absorbed solar energy to those synthetic reactions was discovered. The use of porphyrins by nonphotosynthetic organisms is widespread, and almost certainly random variation in structure led to the discovery that small changes in the porphyrins, leading to the construction of chlorophyll and its use in transmitting energy for biosynthesis, led to the invention of photosynthesis.[19]

Strictly speaking, the primitive synthesis of which we spoke, making use of ultraviolet light or ionizing radiation, is a form of photosynthesis

and in all probability there existed a parallel evolutionary development of this kind of energy conversion process.[20] In fact, modern work, by physical chemists on the effect of the far ultraviolet light on some of the simple molecules we spoke of earlier as constituting the primitive atmosphere of the earth has demonstrated experimentally the feasibility of the idea of the conversion of water (H_2O) into hydrogen (H_2) and oxygen (O_2). It has been possible to demonstrate the conversion of carbon dioxide (CO_2) into carbon monoxide (CO) and oxygen (O_2) using sunlight of such a high energy that very little of it penetrates down very far into the present earth's atmosphere.[21]

Whether the conjunction of the use of visible light-absorbing substances, such as the porphyrins, with the biosynthetic demands of the more highly evolved chemical systems took place before or after the appearance of what we would today call living organisms, matters little for the purposes of our present discussion, important though the question may be. It seems quite clear, however, that these two parallel lines of development did meet, as mentioned earlier, giving rise to the very efficient energy conversion processes resembling those which we know today. It is not unlikely that the final step in the development of modern photosynthesis, namely, the evolution of oxygen, did not take place until relatively late in the sequence of events. For example, we do have organisms today which are capable of using solar energy, via the agency of porphyrin-type molecules, but using other methods of taking care of the oxygen by combination with suitable reducing agents such as hydrogen. These appear in the form of photoreducing organisms such as the photosynthetic bacteria. They dispose of the oxidizing fragment of the water molecule, made by the absorption of light, by combining it with whatever reducing materials may have been present in the primitive atmosphere. It is not until the higher green plants appear that we find the ability of disposing of this oxygen back into the atmosphere as molecular oxygen back into the atmosphere

as molecular oxygen.

THE FOSSIL RECORD -- MAN'S PLACE

With this biological discovery the stage was set for the enormous development of living organisms on the surface of the earth as we know them today. From here on, the fossil record is quite complete and there is little point for us to pursue in detail the ascent and divergence of life, leading ultimately to mankind in the last million years.[22]

It is perhaps worthwhile at this point to try and assess the amount of time which may be allotted to each of the major kinds of operations, or sequences of events, which we have outlined as leading ultimately to cellular life as we know it on the earth today, and man. Most of you are undoubtedly aware of the fact that from the very beginning the fossil record contains evidence of very nearly all of the major subkingdoms, or phyla, of life today. This fossil record, which is some 500 to 1000 million years old, thus indicates that by the time life was sufficiently well developed to leave a fossil record it had already manifested itself in nearly all of the major types of forms which we now recognize. This time period constitutes something less than one-quarter of the entire habitable life span of the earth. Thus we have some two or three billions of years during which we can pursue the process of Chemical Evolution, overlapping with that part of the evolution of cellular life (biotic evolution) which was unable to leave a record of itself in the rocks. This is an extremely long period of time which gives us ample opportunity for the enormous numbers of trials and errors which would be required to develop all the possible molecular processes and combinations which must have been tried.

Undoubtedly, many different information-carrying molecular species had a birth, a life span and a death, much as we know see in the fossil record for the higher forms. One (DNA) or only a few, of these closely related information-carrying molecules, or molecular species, eventually superseded all the rest, be-

because of the particular structural, chemical and dynamic properties of this arrangement of atoms, i. e., stability, template or complementarity quality, mutability and others not yet defined. It was from this (these) that the present-day organism have developed, thus providing a basic similarlity in all living processes as we know them today.

The determinism in the arrangement of a system increases with the number of trials (events) that can occur in reaching it. On the molecular level, where the number of changes occurring per second is high, predictability with regard to what will happen in a given situation to a group of molecules amounts to certainty. For example, pressure maintained by bombardment of molecules on the walls of a vessel containing a certain number of gas molecules at a specified temperature is quite predictable. While we cannot specify the particular molecules which will strike the wall at any time, we can be quite sure that in a given period of time a certain number will do so.

At the other extreme, the segregation and recombination of genes which may take place in the formation of a new individual by (geologically) modern genetic mechanisms appears as a completely undetermined, or random, choice, since only a single event is involved. However, among a group of organisms of a given species there will be a predictable distribution of properties at a given time under a specified set of conditions.

On the other hand, coming up from molecules and molecular aggregates, we will reach a stage, probably after the invention of cellular heridity based on nucleic acid, when the number of events (rate multiplied by time available) will not be large enough to insure that all arrangements possible will have been tried, and an indeterminism with respect to those that have appeared will ensue.

Therefore, while an indeterminism exists with respect to the character of any individual living thing and a limited indeterminism exists with respect to species, the time element is so great and the amount of genetic material which

has been cycled through the sequence of birth, growth, development and death is so enormous,[23] that the certainty of the occurrence of cellular life as we know it on earth today seems assured, given the initial starting conditions.

A most convincing demonstration that such a sequence of events, leading from nonliving matter to life, could, and probably did, take place, would be an experiment in which a system of organic material, called alive by most biologist, is produced through the agency of no other life save the hand of man.[24] And already today there is serious discussion as to whether some of the experiments performed in the last year might not fulfill these conditions.

It thus appears that man is a rather late and highly developed (perhaps the most highly developed) form of that organization of matter which we call living, on the surface of the earth, and which is the result of the peculiar and special environmental situation provided on the surface of the earth since its formation some five billion years ago. We have known for some time now that the earth is the number three planet in orbit around a rather ordinary star on the edge of one of the minor galaxies of the universe. Thus, presuming life to be a unique occurrence limited to the surface of this one rather trivial (in terms of mass, energy, position, etc.) planet in the universe, man, though an impressive representative of the state of matter called living, is not viewed as a major cosmic force.

LIFE ON OTHER PLANETS? -- A COSMIC INFLUENCE

Now man is about to send back into space some bits of the dust from whence it originally came. This return will be in the form of machines, and eventually of man himself. It is thus not only timely but more significant than ever before to ask again the question: What are the probabilities that cellular life as we know it may exist at other sites in the universe than the surface of the earth? In view of the chemistry of carbon (and a few of its near neighbors) and the consequences this has given rise to in the environment to be found on the surface of the earth, all that is required to answer, or to

provide some kind of answer to this question, would be an estimate of the number of other sites, or planets, in the universe which might have the environmental conditions within the range to support cellular life as we know it on the surface of the earth.

Here we follow Shapley[6a] (as well as others[6b]) who begins his calculation with an estimate of the minimum number of stars which might be in the universe. His minimum calculation, based upon the best telescopes we have today, is of the order of 10^{20}, that is, one with twenty zeros after it. The next step is to determine what fraction of these stars will have a planetary system. To make this estimate one must have some concept of how our planetary system was generated. Here there are many theories and Shapley lists fourteen of fifteen of them. However, there are a number of conditions which must be fulfilled and these, taken together with the fact that the universe has been expanding, and some five billion years ago when the planetary systems were formed the universe must have been much more crowded than it is today, gives the figure one in a thousand as a very conservative estimate of the number of stars which have a planetary system.

The next question which Shapley attempts to answer is what fraction of these planetary systems will contain a planet at approximately the correct distance from its star such that it will have a temperature variation compatible with the cellular life that we are seeking to determine. Here, again, we arrive at the very small, and what we consider conservative, figure of only one of these planetary systems in a thousand as containing a planet at approximately the right distance from its sun. The next circumstance which must be fulfilled is that of size. Again, the planet must be of the correct size to retain an atmosphere and not be too large. Here Shapley gives the figure of one in a thousand as a conservatively small fraction.

Finally, of all of these planets which are the correct size, which of them will have the proper atmosphere containing carbon, hydrogen, nitrogen and oxygen, which will be required to give rise to cellular life as we know it on earth? The answer is, again, the very conservative number of only one in a thousand.

Thus, we have four factors of one-thousandth by which we must multiply our figure of 10^{20} (the minimum number of stars which might be in the universe). This leads to the number 10^{8}, that is, one hundred million, as the number of habitable planets to be found in the universe. Remember that this calculation is limited to those planets which will have conditions within the range compatible with cellular life, based on carbon, as we know it on earth. This does not include such systems, which conceivably we can imagine, based on other elements, such as silicon, or nitrogen, or perhaps even anti-matter. Such worlds and such systems may very well exist. However, these are not included as possibilities in this calculation. We have already cut down the limits by our four factors of one-thousandth, leading to something of the order of 100,000,000 planets which can support cellular life as we know it on the surface of the earth.

Since the time element seems to be about the same for all parts of the universe, namely, something greater than five billion years, it would appear that we can be reasonably certain that these hundred million other planets will indeed have cellular life on them. Since in the course of the chemical and biotic evolution the appearance of man on the surface of the earth has occupied only a very small fragment of time, namely, only one million years of the five billion, it is clear that we may expect to find cellular life, and perhaps precellular life and posthuman life, in many of these other planets. The one million year period, given to the evolution of man on earth, constitutes an extremely small element of this long period of time and an uncertainty of this

order could, and almost certainly does, exist in the status of the evolutionary sequence elsewhere in the universe.

We can thus assert with some degree of scientific confidence that cellular life as we know it on the surface of the earth does exist in some millions of other sites in the universe. This does not deny the possibility of the existence of still other forms of matter which might be called living which are foreign to our present experience.

By answering our second question in this way, we have now removed life from the limited place it occupied a moment ago, as a rather special and unique event on one of the minor planets around an ordinary sun at the edge of one of the minor galaxies in the universe, to a state of matter widely distributed throughout the universe. This change induces us to re-examine the status of life on the surface of the earth. In doing so we find that life on the surface of the earth is not a passive, existing thing, but actually changes and forms the environment in which it grows. The surface of the earth has indeed been completely transformed in its character by the development of the state of organization of matter which we call life. Furthermore, it is undergoing another, and perhaps a more profound transformation, by one representative, or manifestation, of that organization of matter, mankind.

MAN IN SPACE -- THE NEXT STEP

Now that man has the capability of taking his machines and himself off of the surface of the earth and of beginning to explore outer space, there is no reason to suppose that life, and man as its representative, will not transform any planet, or any other astral body upon which he lands, in the same way, and perhaps even in a more profound way, than he has transformed the surface of the earth. For example, it might suit him in the future to change the course of the orbit of the moon and it seems within the realm of possibility that he should be able to do so. When we realize that other organisms may

be doing similar things at some millions of other regions in the universe, we see that life itself becomes a cosmic influence of significant proportions, and man, as one representative of that state of organization of matter, becomes a specific cosmic influence himself. Thus have we come to a complete inversion of our view of the place of life and of man in the universe from a trivial to a major cosmic influence. And we have come to this view entirely upon the basis of experimental and observational science and scientific probability.

Man's adventure into space, which is about to begin, is not merely a flexing of muscles -- a demonstration of strength. It is a necessary aspect of evolution and of human evolution in particular. It is an activity within the capability of this complex organism, man, and it must be explored as every other potentially-useful evolutionary possibility has been. The whole evolutionary process depends upon each organism developing to the greatest extent every potential. It is the particular function of the university to facilitate this development of the uniquely human potential of understanding and control -- to lead lead the species in its new exploration as well as serving it in transmitting its established patterns.

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